Results: Patients have had a median of 10 to 124 ECP treatments. The median number of treatments that enabled initial ECP schedule taper was 22(10–124) and to achieve a CR was 62 treatments. Objective response was achieved 61% of patients (CR in 2 patients at 8 and 15 months; PR in 6 patients). Fifteen percent had stable disease and 23% progressed. At the time of this report 6 patients are still receiving ECP. Refer to table for organ-specific response. Of note, six of 10 patients with lichenoid GVHD and 3 of 4 with sclerotic GVHD improved. Nine patients have been able to taper corticosteroids≥50% from starting dose. Five patients have died (3 with progressive GVHD, 2 with infection/GVHD).

ECP is an alternative effective method to treat moderate to severe SR cGVHD in pediatric patients. ECP has allowed for significant corticosteroid sparing. Prospective studies are necessary to determine optimal schedule and durability of response.

Response by Organ

System	Manifestation	N	CR	PR	SD	PD
Skin	Rash/Lichenoid	10	2	4	4	-
	Fasciitis/Scleroderma	4	1	2	1	-
Oral	Symptoms/ lichenoid/erythema	9	2	7	-	-
Ocular	Symptoms/need for treatment	3	1	1	1	-
Joints	Arthralgias/ Contractures	5	2	1	2	-
GI	Vomiting/Abdominal Pain/Diarrhea	3	-	1	2	-
Liver	Bilirubin > 2	8	1	2	3	2
Pulmonary	Worsening symptoms/PFTs	4	-	1	2	1

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PRELIMINARY RESULTS OF A PHASE I STUDY OF IMMUNO-CHEMOTHERAPY (CTX) CONDITIONING WITH GEMTUZUMAB OZOGAMICIN (GO), BUSULFAN (Bu) AND CYCLOPHOSPHAMIDE (Cy) FOLLOWED BY ALLOGENEIC STEM CELL TRANSPLANTATION (AlloSCT) IN PEDIATRIC RECIPIENTS WITH HIGH RISK (HR) CD33+ ACUTE MYELOGENOUS LEUKEMIA (AML)

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Survival following AlloSCT for HR AML (≥CR3, induction failure [IF], refractory disease) is dismal (≤10%). BuCy is standard conditioning in children with good risk AML (Woods et al, Blood, 2001). CD33 is expressed in 80–90% of childhood AML (Creutzig et al, Blood, 1997). GO, an anti-CD33 immunotoxin, induces remission in 20–30% of relapsed/refractory childhood AML (Arceci et al, Blood, 2005). We have reported the safety of GO as post-consolidation therapy after reduced intensity conditioning alloSCT in good risk childhood AML (Roman et al, Clin Can Res, 2005). In this study, we explore the feasibility and safety of combination immuno-CTX conditioning with GO and myeloablative (MA) BuCy followed by alloSCT in pediatric recipients with HR CD33+ AML. Nine patients, median age 8 yr (0.75–17 yr) with HR CD33+ AML (1 CR3, 5 IF, 3 refractory disease) were studied. Donor sources were: 1 6/6 HLA-matched sibling peripheral blood stem cell (PBSC), 1 10/10 matched unrelated donor (MUD), 7 umbilical cord blood (UCB) (2 6/6, 2 5/6 and 3 4/6). Conditioning was GO on day -14, Bu (12.8 mg/kg if age > 4 yr; 16 mg/kg if age < 4 yr) day -7 to -4 and Cy (120 mg/kg) day -3 to -2. Unrelated alloSCT recipients received rabbit antithymocyte globulin (8 mg/kg) from day -5 to -2. GO was given as a dose escalation; 3 patients each received 3 mg/m^2, 4.5 mg/m^2 and 6 mg/m^2. All patients received enoxaparin (1 mg/kg) from day -15 to +21 as prophylaxis for sinusoidal obstruction syndrome (SOS). There has been no GO dose limiting toxicity to date. Mean neutrophil and platelet engraftment in all patients was on day 24 ± 10 (n = 8) and day 54 ± 49 (n = 7), respectively. In the UCB group, mean neutrophil and platelet engraftment was on day 28 ± 8 (n = 6) and day 64 ± 56 (n = 5), respectively. Mean donor chimerism on days 30 and 60 was 96% ± 5 and 96% ± 10, respectively. One patient (GO dose 4.5 mg/m^2) developed mild SOS on day 33 that resolved without therapy. One patient died of extensive chronic graft vs. host disease on day 269 and 4 of progressive disease (day > 200), while 4 are surviving recurrence-free at a median of 52 months. Combination immuno-CTX conditioning with GO and MA BuCy followed by AlloSCT has been well tolerated to date in children with HR CD33+ AML and resulted in ≥95% donor chimerism. The maximal tolerated dose (MTD) of GO as part of a preparative regimen for MA alloSCT in children with CD33+ AML has yet to be determined. We are currently accruing patients at the next dose level of GO (7.5 mg/m^2).

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UNRELATED DONOR UMBILICAL CORD BLOOD TRANSPLANT FOR HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Familial Hemophagocytic Lymphohistiocytosis (HLH) is a rare disorder of immunoregulation that is usually fatal if untreated. Characterized by fever, hepatosplenomagaly, CNS disease, coagulation disorders, pancytopenia and hemaophagocytosis, onset is usually prior to age 1. Stem cell transplant (SCT) is the only curative option, however, most children lack suitable matched related donors. Umbilical cord blood (UCB) is banked and rapidly available, and it has a lower incidence of acute and chronic GVHD and less viral contamination when compared with adult stem cell sources. HLH is a disease of infants, so UCB cell dose is not a limiting factor. All of these features make UCB an attractive stem cell source for transplantation in this patient population, however there are few reports of UCBT for HLH. Here we report the results of 10 children treated at Duke University Medical Center and the University of Florida with HLH who underwent unrelated donor UCBT between 1994 and 2007. Seven girls and 3 boys received their UCBT at a median of 6 months of age, with all but one having well controlled disease prior to transplant. Treatment prior to UCBT was with VP-16, cyclosporine, and decadron. The preparative regimen consisted of busulfan (Bu), cyclophosphamide (Cy)/Etoposide (VP-16)/antithymocyte globulin (ATG) in the 4 most recent patients, and Bu/Cy/ATG in 6. All children successfully achieved neutrophil engraftment at a median of 17 (range 13–26) days. The median time to platelets greater than 50,000 was 53 days, and PRBC independence was 41 days. Four children experienced grade I, 1 grade II, 1 grade III and 1 Grade IV acute GVHD, while the remainder had none. All children with grade II-IV GVHD received steroids and the child with grade IV GVHD also received daclizumab. Other complications included veno-occlusive disease (VOD) in 4 children, and infections. Eight of 10 children (80%) are surviving event free for a median of 7 years post transplant. One died at day + 30 of hepatic failure attributed to VOD and GVHD, the other at day + 72 of pulmonary hemorrhage, CMV and Parainfluenza pneumonia. Survival following SCT for HLH is reported in many series at 50–60%. VOD, organ damage and GVHD are significant contributors to morbidity and mortality. In combination with initial HLH treatment, UCBT with a standard myeloablative, chemotherapy-based preparative regimen appears promising, providing an 80% event free survival in this pilot patient population.

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CO-INFUSION OF MATCHED SIBLING DONOR CORD BLOOD AND BONE MARROW AS STEM CELL SOURCE FOR ALLOGENEIC STEM CELL TRANSPLANTATION IN PEDIATRIC NON-MALIGNANT DISORDERS

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